

REMARKS

Status of Application

Claims 3-19 were pending in this application. Claims 3-7 were withdrawn and claims 8-19 were rejected.

By this amendment, claims 8, 12, 16, and 20-28 are pending as new or previously presented. Claims 9-11, 13-15, and 17-19 are cancelled. No new matter is introduced by these amendments.

Applicant requests reconsideration and allowance of claims 8, 12, 16, and 20-28, and rejoinder of appropriate method claims.

Applicant reserves the right to prosecute any withdrawn, cancelled, or non-elected claims and/or subject matter in separate applications.

35 U.S.C. § 112 Rejections

Examiner rejected claims 9-11, 13-15, and 17-19. These claims have been cancelled in favor of device claims 20-28 which moot the rejections.

35 U.S.C. § 103 Rejections

Examiner rejected pending claims 8, 12, and 16 as being unpatentable over Armour Pharmaceutical Company (EP 0115627) ("APC"), and Azria et al., U.S. Patent 5,759,565, both already of record, and newly cited Grebow et al. U.S. Patent 5,026,825.

In the previous response, Applicant submitted that Azria et al. purposefully and intentionally teach away from use of chlorobutanol in a calcitonin solution by showing specific and credible evidence that chlorobutanol does not sufficiently destroy microorganisms in a calcitonin solution. Further, Applicant submitted that the APC reference (EP '627) is not pertinent because it provided no specific factual evidence on which a person of ordinary skill in the art could have relied in 1998 when the unsuitability of chlorobutanol was shown in fact by Azria et al. Thus, Applicant submitted that a person of ordinary skill in the art in 1998, in view of Azria et al., would have been strongly dissuaded from using chlorobutanol in a calcitonin nasal spray, and would have been led to use the working alternative benzalkonium chloride which Azria et al. showed was operable. This is a clear teaching away from selecting

chlorobutanol as a preservative in a calcitonin solution. Azria et al. expressly disparaged the use of chlorobutanol and successfully demonstrated the use of an alternative.

In the office Action mailed October 29, 2007, Examiner turned to the newly cited reference Grebow et al. U.S. Patent 5,026,825 for its disclosure of chlorobutanol in a calcitonin formulation at a concentration of 0.1%(w/v), which Examiner stated is “lower than that of the Applicants.” The Examiner concluded that Grebow et al. somehow provided new evidence of the suitability of chlorobutanol in a calcitonin formulation.

Applicant respectfully submits that Grebow et al. adds no new information whatsoever to the discussion and does not obviate the teaching away expressly recited in Azria et al. Grebow et al. discloses “preservatives” at column 11, line 50, and provides a list of eight or more possible preservatives including chlorobutanol at column 12, lines 1-16. Lastly, Grebow et al. discloses numerous prophetic formulations of calcitonin, one of which recites chlorobutanol at 0.1%(w/v) (column 13, line 14). But no working examples in Grebow et al. show the use of chlorobutanol.

The information disclosed in Grebow et al. does not go beyond that found in the APC reference which was discussed in Applicant’s previous response. To wit, the APC reference also discloses a prophetic formulation of calcitonin with chlorobutanol at 0.1%(w/v) (page 10).

Moreover, the information disclosed in Grebow et al. does not reduce the force of the teaching away expressly described in Azria et al. Importantly, both Grebow et al. and the APC reference were published long before Azria et al. Because Azria et al. provided specific and credible test results showing that chlorobutanol does not sufficiently destroy microorganisms in a calcitonin solution, this fact would have been reasonably relied upon by a person of ordinary skill in the art. Neither Grebow et al. nor the APC reference provide any information that would cast doubt on the laboratory test results of Azria et al. Thus, a person of ordinary skill in the art in 1998 or later, in full view of the published results of Azria et al., would have been strongly dissuaded from using chlorobutanol in a calcitonin nasal spray, and would have been steered to the operable alternative benzalkonium chloride.

In sum, the prophetic disclosures of Grebow et al. and the APC reference are far outweighed by the specific and credible factual evidence of Azria et al. that chlorobutanol does not sufficiently destroy microorganisms in a calcitonin solution. Further, in light of the

Declaration of Henry R. Costantino submitted previously by Applicant, which states that chlorobutanol was found to be acceptable as an antimicrobial in a calcitonin composition, and which further states that in view of Azria et al. there would have been no reasonable expectation of success of using chlorobutanol in a calcitonin nasal pharmaceutical composition, it is clear that Applicant's discovery that formulations of calcitonin salmon containing chlorobutanol have acceptable antimicrobial effect shows that claims 8, 12, and 16 are patentable over the cited references, either alone or in any combination.

In conclusion, Applicant respectfully points out that Examiner's second search of the prior art did not reveal any pertinent information beyond that already considered. Applicant respectfully submits that claims 8, 12, and 16 are in condition for allowance and requests consideration of device claims 20-28 which are based on Applicants' patentable calcitonin formulations.

Should there remain any unresolved issue that would require an adverse action, it is respectfully requested that Examiner telephone Applicant's attorney so that such issue may be resolved as expeditiously as possible.

Should the U.S. Patent and Trademark Office determine that any additional fee is due, or that a refund is owed for this application, the Commissioner is hereby authorized and requested to charge the required fee and/or credit the refund owed to Deposit Account No. 502769.

Respectfully submitted,

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